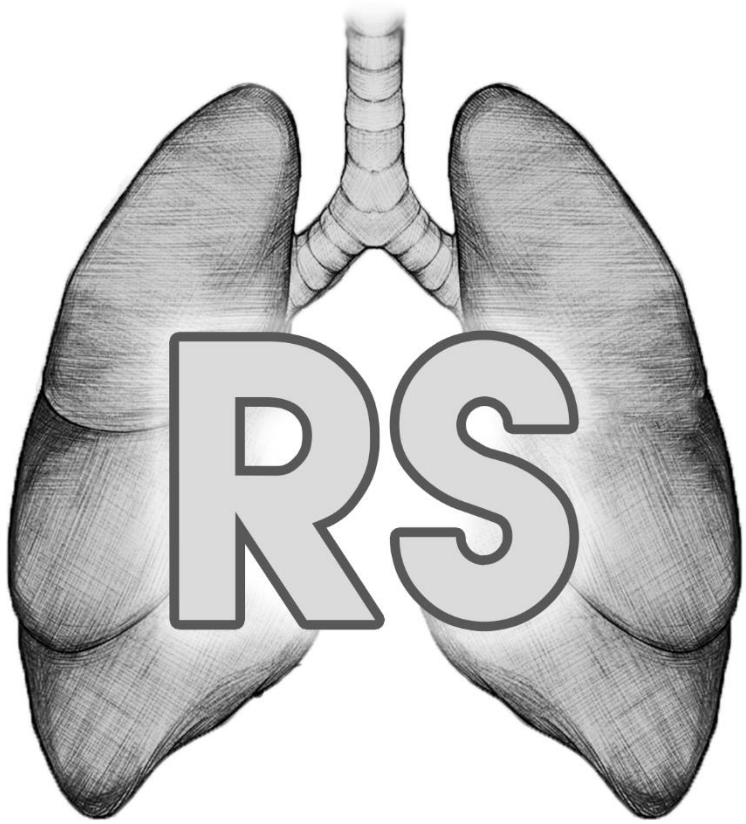

PHYSIOLOGY

☑ Sheet ○ Slide ○ Handout

Number

6

Subject

Diffusion capacity and V/Q ratio

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Date: 2/12/2016

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Overview about obstructive and restrictive diseases:

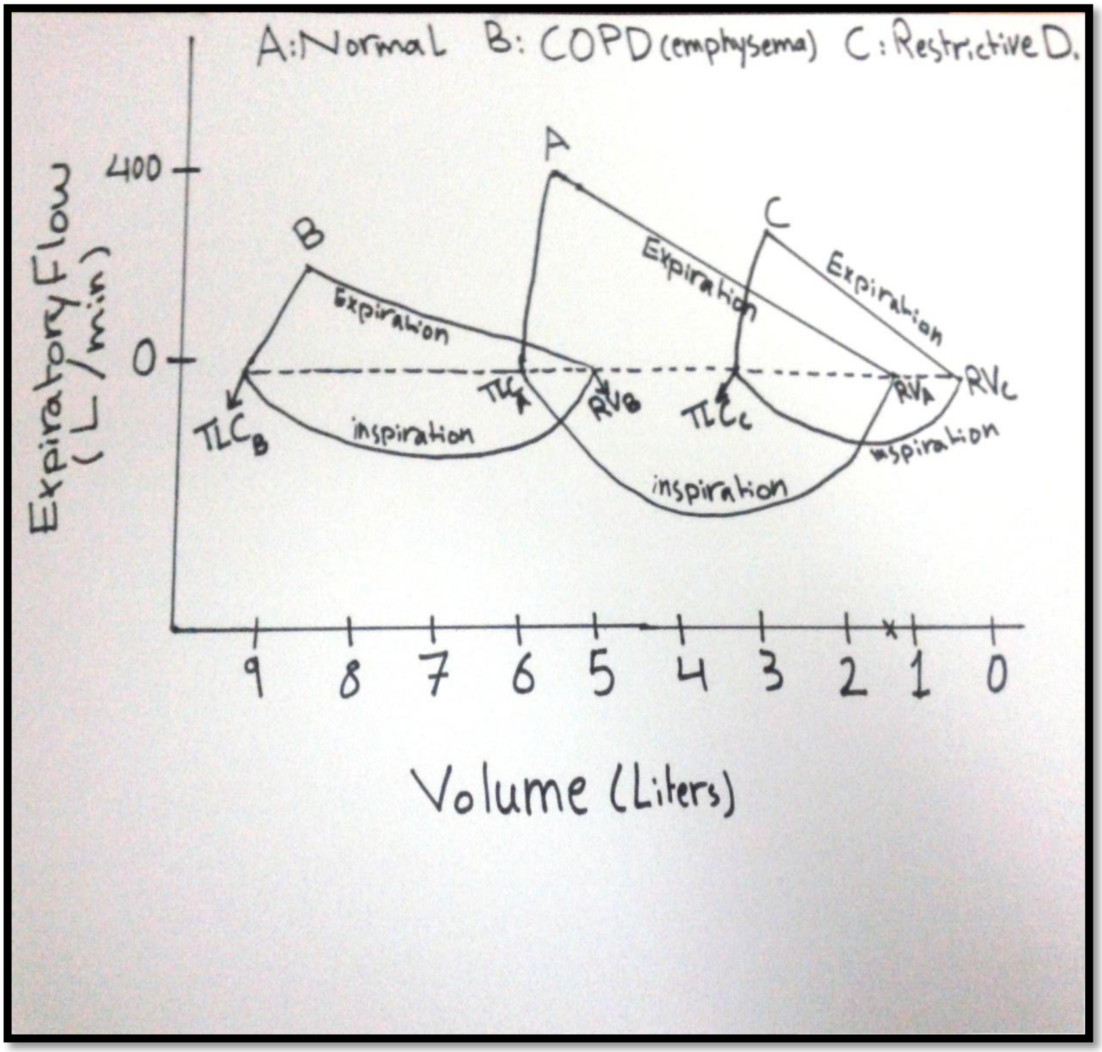
To differentiate between obstructive and restrictive diseases, usually, we ask patients to inflate their lungs maximally reaching total lung capacity (TLC) then to deflate them reaching the residual volume (RV) forcefully and by this procedure we get *the maximum expiratory flow rate (around 400 L/min normally).*

To deal well with the figure (1-6) in the next page; imagine that you fill your lungs to TLC and start to exhale the air so, the line ascends to reach a peak that represents the maximum expiratory flow rate then starts to decline as you are emptying the lungs until you reach RV where the expiratory flow equals zero, then you take inspiration forcefully creating a loop called *maximum flow-volume loop* (under the zero line) to return back to TLC.

In obstructive disease such as emphysema (B, figure 1-6) , the maximum expiratory flow rate is less than normal because the patients can not exhale the air easily due to increase in airway resistance even the *TLC and RV is higher* than normal. *The ratio (FEV1/FVC) is less than 0.8.*

On the other hand, **in restrictive disease** such as pulmonary fibrosis (C, figure 1-6), there is no problem in airways but the forced expiratory volume (FEV1; 1 refers to "within 1 second") is low and the forced vital capacity (FVC) is also low consequently the ratio (FEV1/FVC) will be around 0.8 and sometimes is higher, so in restrictive disease *this ratio equals or higher than normal (0.8).*

In restrictive disease, *TLC and RV is lower than normal* but the maximum expiratory flow is higher than normal at **comparable volumes**; for more explanation look at the figure (1-6) , let us assume that the volume 2.5 L and draw a perpendicular line from x-axis (2.5) to intersect the graph A and graph C (above the zero line) you can notice that the expiratory flow for C is higher than that for A and this is because the collapsing forces are really high in patients with restrictive disease, **so what makes the maximum expiratory flow rate in this condition less than normal is the low total lung capacity (TLC)**.



Figure(1-6): represents the respiratory flow (here, we focused on the expiratory flow which is above the zero rather than the inspiratory flow) on the Y-axis and air volume in lungs on the X-axis.

Respiratory membrane:

Actually, we have too much lung in terms of function since at the first third of capillaries around the alveoli of lungs, we reach the partial pressure of O2 equaled to 100 mmHg and after that no gas exchange occurs since the pressure gradient now is zero.

If someone works in a place filled with phosphate dusts, he will inhale them and become more susceptible to silicosis, asbestosis, tuberculosis, pneumonia and pulmonary fibrosis, in such conditions this person should not wait the symptoms related to lung disease to appear and then go to the doctor, this person should do an early diagnosis thus the disease is discovered earlier consequently this person has an excuse to change the work position from the field to the office to avoid the exposing to phosphate dusts. *So before the symptoms appear, I should know if the respiratory membrane is affected before it is too late*.

So, we are going to do a test now to measure the *diffusion capacity* of the respiratory membrane; how much oxygen can diffuse through the membrane from the lung to the blood per minute for every 1 mmHg pressure difference, for example if the normal value for this test is 20 and when you did the test for a person the result was 15, you must suspect that there is a problem even that the reserve compensates.

Diffusion capacity. We want to measure the diffusion capacity for O2 and CO2; and if the diffusion capacity for O2 is 10 then that for CO2 is 200 because CO2 is 20 times more diffusible than O2.

So, in this section we will follow steps to calculate the diffusion capacity for O2 and CO2:

1. Let's start with *ohm's law* which states that flow equals driving force (DF) divided by Resistance(R) ; flow = DF/R:
   a. *Resistance* is an expression describing how much is difficult for a process to occur and the opposite to resistance is the conductance for ions, permeability for glucose and *diffusion capacity (D_L)* for oxygen, so $R=1/D_{L \text{ for a gas X}}$ then flow= $DF*D_L$ *(notice that DL refers to diffusion **L**imited not diffusion capacity of the **L**ung; do not focus on this note because you can refer it to Lung rather than limited).*
   b. *Flow* is something (volume) occurs per time unite and in this situation is the *oxygen consumption V_{O2}* (250mL/min normally at rest).
   c. *DF* is the pressure difference between alveoli and capillary (ΔP_{O2}).

2. So we end up with $D_{LO2} = V_{O2}/ \Delta P_{O2}$; if we measure oxygen consumption and pressure difference for oxygen we can calculate the diffusion capacity:
   a. *It is easy* to measure **oxygen consumption** by the unit of mL/min; you make the patient to breathe in a closed bag with known oxygen volume for 10 minutes then you measure how many oxygen volume is left in the bag, the difference between initial volume and final volume is the volume consumed by the lung and when we divide it by 10 minutes we get the oxygen consumption.

b. *It is difficult* to measure the **pressure difference for oxygen** because it is not easy to get the pressure in *the whole capillary (not just the first one third)* that surrounds the alveoli (P_{O2} in alveoli = 100 mmHg); so at the beginning of the first third of capillary (at the arterial end of pulmonary capillary) the partial pressure for oxygen equals 40 mmHg and starts to increase until we reach the end of this third where the pressure for oxygen equals 100 mmHg ,so the pressure difference at the beginning is 60 mmHg and at the end is 0 mmHg. Then we apply the same principle on the other two thirds where at the beginning and at the end the pressure difference equals 0 mmHg because after the first third we reach a pressure for oxygen 100 mmHg. After that we calculate the average pressure difference for the three thirds (for each third we summate the pressure difference at the beginning and at the end then we divide the result by 2):

- In the first third, the average = (60+0)/2 = 30mmHg.
- In the other two thirds for each one, the average = (0+0)/2 = 0mmHg. So the average for all the three thirds = (30+0+0)/3 = 10mmHg.

But, when we want to measure P_{O2} in the capillary by laboratory procedure, it is difficult to do that due to the fact that gas exchange occurs only in a small part of the capillary, while the rest of the capillary is under equilibrium.

3. To solve the problem in point 2.b, we have to discuss the following:

Diffusion capacity for gas X:
$D_{LX} = (A / d)_{membrane} * (S / \sqrt{M.W})_{gas\ x}$
In this equation:
A: represents the surface area of diffusion for the membrane (in the lung is around 50-100 m^2).
d: represents the membrane thickness.
S: represents the solubility of the gas X.
M.W: represents the molecular weight for the gas X.
(S/square root of M.W): represents the diffusion coefficient (D) for gas X.

So, the higher in A, the lower in d, the higher in ΔP, the higher in S and the lower in M.W is the higher D_L and vice versa. Notice that we have square root of M.W not the molecular weight itself which means when we take for example the square root for O2 (square root of 32 =5.65) and that for CO2 (square root of 44=6.63), there will be negligible difference between the two values.

Diffusion coefficient (D) for O2 is the reference point and we assume that it is 1 and that for CO2 and CO is 20 and 0.8 respectively (this is because the solubility of CO2 is 20 times more than O2 and the solubility of CO is 0.8 the solubility of O2 and the square root of M.W has minimal effect on D). Actually, these values are not the true values; they are relative to oxygen when we assumed its D was 1. And because the Respiratory membrane is the same for O2, CO2 and CO, we can conclude that D_{LCO2}=20 D_{LO2} and D_{LCO}= 0.8 D_{LO2}. (You have to memorize these numbers)
Now, the **strong question** is*" how can what discussed in point3 solve the problem in point2.b?"* the answer is in point 4.

4. We calculate D_{LO2} indirectly by measuring D_{LCO} (D_{LCO}=0.8D_{LO2}); CO has **250 times** much higher affinity to bind hemoglobin than O2 in other words; when we have a mixture of O2 with pressure **100mmHg** and CO with pressure **0.4 mmHg**, 50% of saturated hemoglobin is saturated with CO and the other 50% will be for O2 (notice that 0.4*250=100). So a pressure for CO equaled to 1mmHg is enough to cause death.
   When a person inhales an air containing CO with very low partial pressure and diffuses from the alveoli to blood, it will bind hemoglobin with high affinity making its pressure in the blood plasma almost zero and because we can *easily measure its partial pressure in alveoli*, so the pressure difference for CO is easily calculated as $P_{CO\ Alveoli}$-$P_{CO\ in\ blood}$ = $P_{CO\ alveoli}$ – zero =$P_{CO\ alveoli}$.
   Then CO consumption (V_{CO}) is easily calculated, consequently D_{LCO}=V_{CO}/$P_{CO\ alveoli}$ and if the D_{LCO} is 17 then D_{LO2} =17/0.8=21.25. The problem is finally solved.

Importance of measuring the diffusion capacity for respiratory membrane. By measuring the D_L, the physician can diagnose any defect in the respiratory membrane before it is too late. For example, for workers who are exposed to phosphate dusts making them susceptible to lung diseases. Also, it is used in choosing players such as: marathon runners and weight-lifters; marathon runners should have slow red fibers, high cardiac reserve and *high diffusion capacity for oxygen* while weight-lifters and 100m-runners should have fast white fibers and it is not necessarily with high cardiac reserve *neither high diffusion capacity* because they depend on anaerobic pathway to get energy rather than aerobic pathway since it is slow and not useful in such conditions so the ATP source from phosphocreatine is enough.

Ventilation-perfusion ratio:

We expect from the respiratory system two things: (1) adequate ventilation (V). (2) adequate perfusion (Q) which is corresponded to blood flow; we don't want perfusion without ventilation (wasted perfusion) and we don't want ventilation without perfusion (wasted ventilation).

Usually, we refer the perfusion to Cardiac output (CO) and we have two types of ventilation: (1) *pulmonary ventilation* =tidal volume (V_T) * respiratory rate (RR) =0.5*12=6L/min (2) *alveolar ventilation*= (tidal volume-anatomic dead space volume (ADSV))*Respiratory rate (RR) = (0.5-0.15)*12=4.2L/min .

Tidal volume (500mL) is divided into: (1) *ADSV* (150mL). (2) 350 mL which is subdivided into: (a) *alveolar wasted volume (AWV):* the volume that is ventilated but not perfused (zero mL; normally). (b) the volume that is ventilated and perfused (350 mL; normally).

In lung diseases, AWV is higher than zero, so we end up with two volumes are wasted: ADSV and AWV and the summation of the two volumes gives me a volume called *physiological dead space volume (V_D)*.so, V_D=ADSV+AWV, according this equation V_D is never less than ADSV; it must be equaled or higher than ADSV (it might be higher if AWV is more than zero).

The ratio (V_D/V_T) is calculated by this equation:

(V_D/V_T)= (P_{aCO2}-P_{ECO2}) / $P_{aCO2;}$ in which P_{aCO2} refers to the partial pressure of CO2 in the arterial blood and P_{ECO2} refers to the partial pressure of CO2 in the entire expired air (normally is around 28mmHg).

Regional variations in ventilation-perfusion ratio (V/Q) in the lung. We take the lung in standing individual dividing it into: (1) apex in which the intrapleural pressure is not the same as we know; it is not -4mmHg but it is -8mmHg which means that the alveoli in the apex are already inflated due to presence of more negative pressure and consequently, it is difficult to inflate them. (2) base in which the intrapleural pressure is less negative equaled to -2mmHg which means that the alveoli in the base are partially inflated and consequently, it is easy to inflate them.

So, <u>most of the 500 mL which they are going to be inhaled is directed toward the base not the apex,</u> *but the initial part of air that is inhaled is directed toward the apex not the base because the intrapleural pressure in the apex is more negative (-8mmHg) which means it is easier to air to be inhaled toward the apex instead of the base but after the alveoli in the apex are completely inflated, it is going to be directed into the base.*

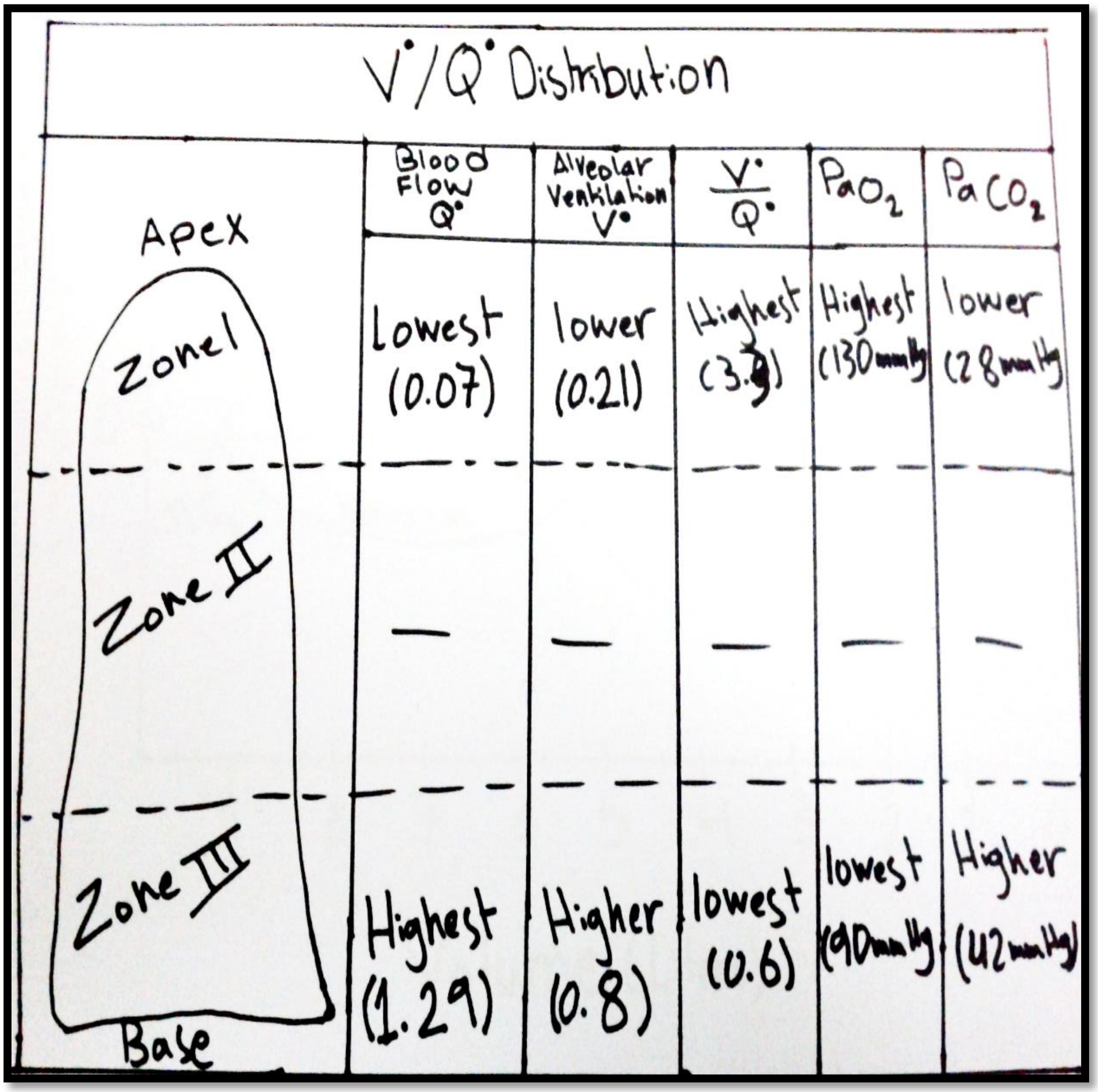
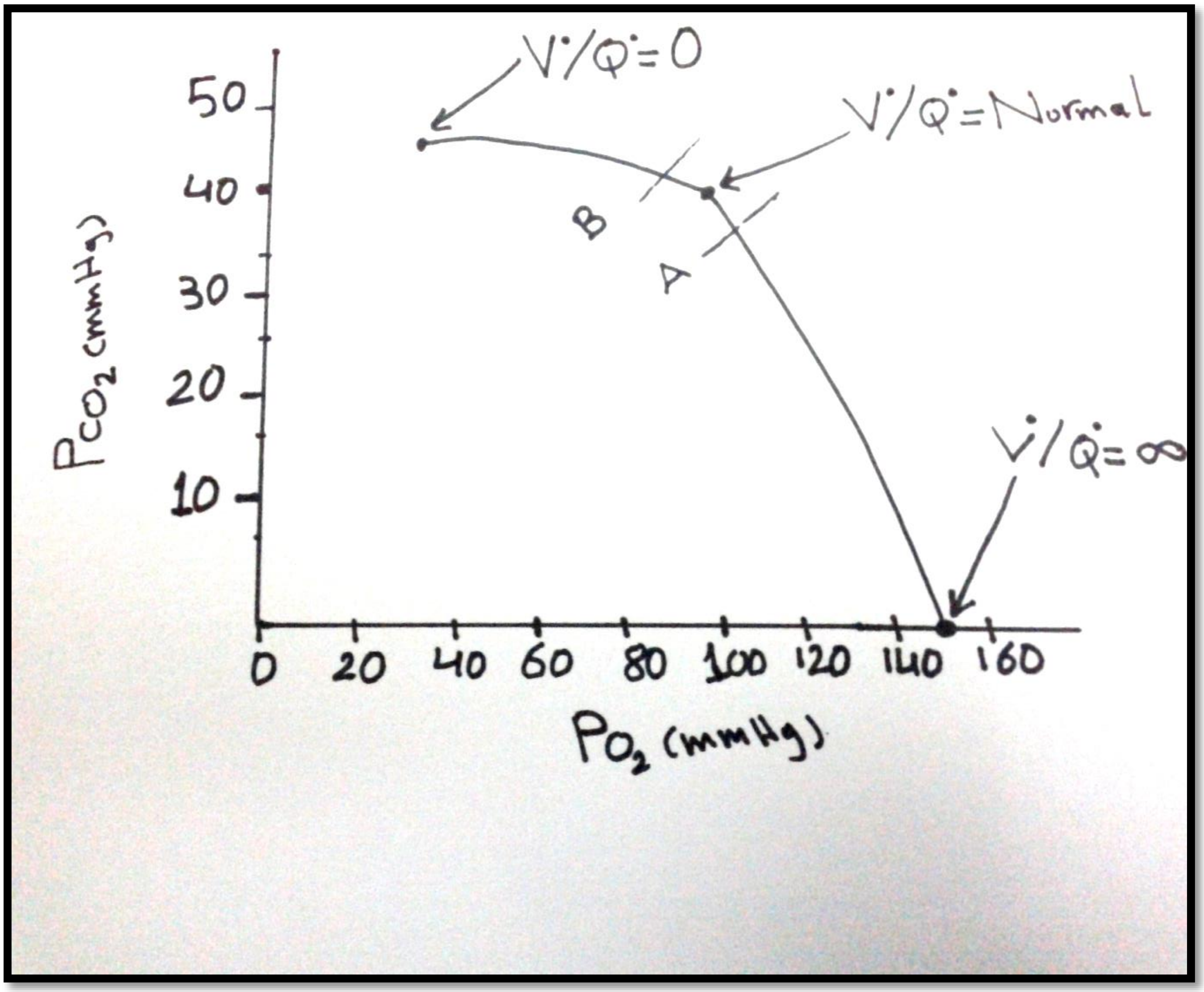


Figure (2-6); represents the regional variations in the lung in terms of ventilation-perfusion ratio.

According to figure (2-6); the heart ejects blood to the apex and the base and the blood is affected by the gravity more than the air, *so the blood goes to the base is more than that goes to the apex* (notice the column of perfusion(blood flow)) . Also, you can notice from the alveolar ventilation column *that ventilation in base is higher than that for apex.* But if you calculate the ventilation-perfusion ratio, you end up with *that the ratio for the apex is higher than the ratio for the base*. *(Do not memorize the numbers in table of figure (2-6)).*

Also, keep in mind that the partial pressure for oxygen in the apex (130 mmHg) is higher than that in the base (90 mmHg).

To understand the principle of V/Q ratio, we will make two assumptions:

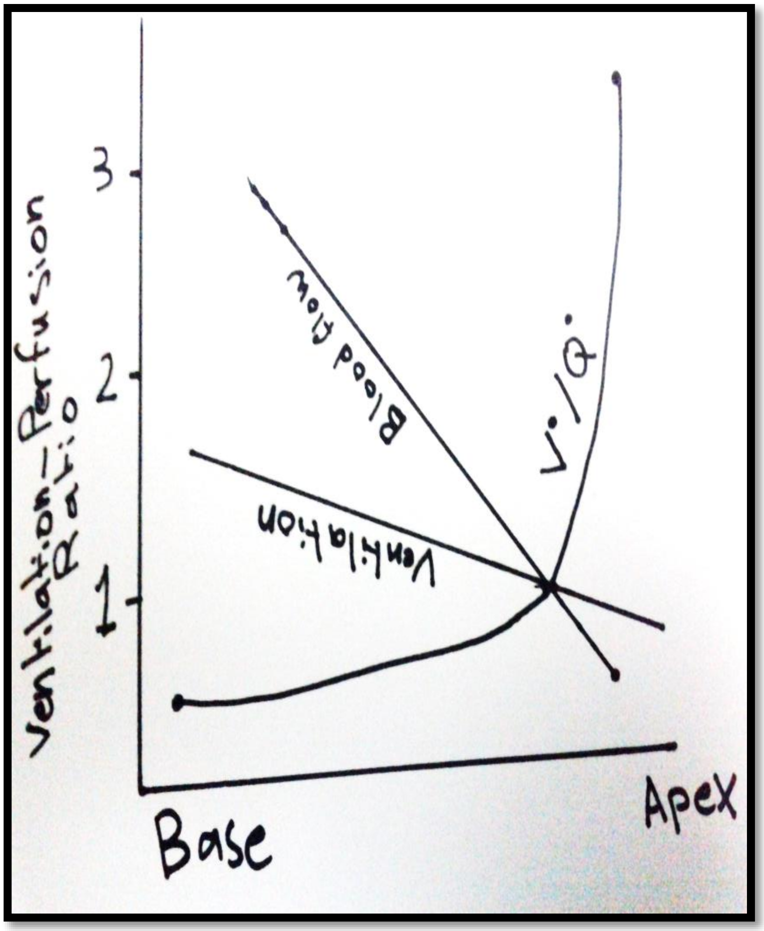


Figure(3-6): represents the ventilation-perfusion ratio-related to the two assumptions below.

(1) The perfusion(Q) around the alveoli is obstructed (let's assume that is zero; no blood flow); so the partial pressure for oxygen in alveoli equals 150 mmHg (the same as the outside but is humidified) and the partial pressure for CO2 in alveoli is zero(the same as the outside). This assumption is corresponded to ratio (V/Q) =∞ in figure (3-6).

(2) The bronchioles are obstructed, so the ventilation (V) equals zero; no air flow comes to alveoli. According to that, P_{O2} in alveoli= 40 mmHg and P_{CO2} in alveoli= 45 mmHg (the same as in the capillary). This is corresponded to (V/Q) =0 in figure (3-6).

Look at figure (3-6) again, and notice the normal (V/Q) ratio; it is located where the P_{O2} =100mmHg and the P_{CO2}=40mmHg. The line A represents the apex of the lung since it is on higher ratio and B represents the base of the lung where the ratio is lower.



Figure(4-6): represents the V/Q ratio distribution in the apex and the base of the lung.

According to figure (4-6); we can say that the blood flow and ventilation in the base is higher than in the apex while the ventilation-perfusion ratio in the apex is higher than that for the base.

Ventilation-perfusion ratio for the whole lung. First we calculate the alveolar ventilation = $(V_T - V_D)$*RR = (0.5-0.15)*12=4.2 L/min and the total blood flow which goes to the lungs through the pulmonary trunk equals the cardiac output (CO)=5L/min, so the ratio equals 4.2/5=0.84.

Clinical note. The partial pressure in the apical alveoli equals 130 mmHg and these alveoli have too much oxygen in addition to high V/Q ratio and from microbiology course we studied that TB bacilli love oxygen; so they tend to reside in the apex of the lung thus when you observe a shadow in the apex then it is TB while if you observe a shadow in the base then it is a cancer unless it is proven otherwise. *We conclude that the shadow in the base is more serious diagnostic sign than the shadow in the apex.*

(Actually, what makes the ratio for the apex is higher than the base is that the blood is affected by the gravity much more than air; so air flow that comes to the apex of the lung is more than the blood perfused to, in addition to that what makes the ventilation lower in the apex is the more negative pressure around the apical alveoli).

The magic of V/Q ratio. One part of the expired air comes from the apical alveoli and three parts comes from the base with total 4 parts ; when we calculate the average partial pressure for oxygen (130+90+90+90/4) = 400/4 =**100mmHg**, the value will be the same as for the alveolar partial pressure for oxygen.

The lecture is over but the sheet is not; there is something more enjoyable in the next page (believe me!!!)

Test yourself- **Veto questions.**

1. A patient with a lung disease, after doing pulmonary tests ; we end up with the following : he only perfuses 60 mL of the ventilated air volume, his respiratory rate equals 20 breath/min, the ratio between partial pressure for CO_2 in expired air to that for CO_2 in the arterial blood equals 0.2 and ADSV = 150 mL. Is this patient receiving adequate alveolar ventilation? Justify your answer.

Answer: the patient is not receiving adequate alveolar ventilation because it equals 1.2L/min.

2. A 54-years old man is in the clinic complaining of weakness, fatigue and difficulty in breathing after muscular exercise , after doing pulmonary and heart-function tests, the physician ends up with the following with regard to the heart: ejection fraction is around 34%, heart rate =80 beats/min, and EDV=190 mL, while pulmonary tests reveal the following: the diffusion capacity of lung for CO is 13, V/Q ratio for the lung equals 0.875 and the difference in oxygen content between pulmonary vein and artery is 45mL/L, answer the following:

a. Is this man receiving adequate alveolar ventilation? Justify your answer.

Answer: this man is receiving adequate alveolar ventilation because it equals 4.5L/min.

b. calculate the driving force for oxygen diffusion

Answer: 14.3 mmHg.

No need for Einstein's quotes because this sheet is full of imagination.

Now, the sheet is over